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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,868	11/28/2001	Cornelia M. Gorman	11669.103USW3	6177

7590 05/08/2006

Attention: Katherine M. Kowalchyk
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EXAMINER	
GUCKER, STEPHEN	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 05/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,868	GORMAN ET AL.	
	Examiner	Art Unit	
	Stephen Gucker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 4/14/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Any objections or rejections made in a previous Office Action that are not herein reinstated have been withdrawn.

3. Claims 32-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods producing chemically or structurally defined prorelaxin (and the isolated host cells that do this), is not enabling for prorelaxin that is not adequately characterized by structural or chemical means, for example, by a SEQ ID NO. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Claims 32-37 still recite "mutants thereof having a conservative amino acid substitution at one or more residues" in an attempt to characterize the nucleic acid encoding the polypeptide. However, the specification only provides adequate support for the nucleotide and amino acid sequence for human prorelaxin, and it is the Examiner's belief that the state of the prior art at the effective filing date of the instant Application (December 6, 1991) was that only rat, shark, porcine and human species of prorelaxin had been successfully sequenced. Therefore, the instant claims are not commensurate with the disclosure, as the claims are overly broad in that they encompass host cells and methods of making all forms of prorelaxin from every animal species, including prorelaxin with unlimited amino acid substitutions (see page 32, line 30 to page 33, line 7 of the specification). Because of the inherent

unpredictability of trying to determine the biological functions of an amino acid sequence with unlimited substitutions, even just conservative ones (see Rudinger, pages 3 and 5-6), the claims are not enabled to their full reasonable scope using the definitions provided by Applicant because undue experimentation would be required in order to determine which domains of the prorelaxin structure could be conservatively substituted multiple times and which domains need to stay invariant in order to preserve biological functionality.

4. Claims 32 and 34-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hudson et al. (US 4,871,670, "Hudson") in view of Mulvihill et al (PTO-1449, filed 6/25/02, EP 319,944, "Mulvihill") for reasons of record and the following. Hudson teaches the nucleic acid sequences for human relaxin and prorelaxin (abstract, Figures 2-3, and columns 15-18) and the transfection of bacteria in order to make the A, B, and C polypeptide chains of relaxin which can then be covalently linked by chemical means to make mature relaxin (column 6, lines 12-59 and column 13, line 14 to column 14, line 40). Hudson does not teach cells or methods using the cleaving endoprotease KEX2 or human embryonic kidney 293 cells. Mulvihill teaches the encoding sequence for KEX2 and methods using 293 cells transfected with KEX2 as a general method to prepare multi-chain polypeptides such as protein C (abstract, page 4, lines 30-48, page 5, lines 35-46, page 7, lines 14-15, page 8, lines 26-40, and pages 14-19) without resorting to the chemical linking steps of Hudson. Mulvihill does not teach host cells or methods of making prorelaxin or relaxin. It would have been obvious at the time the invention was made for one of ordinary skill in the art to make isolated animal host cells that produced

relaxin by using the sequence information from Hudson in the 293 cells transfected with KEX2 as disclosed by Mulvihill for the many advantages taught by Mulvihill for the use of co-expression in mammalian cells as compared to single expression in mammalian cells (abstract, page 2, lines 4-41, and page 4, lines 32-37). Additionally, the fact that the teachings of Mulvihill exclude the use of the cumbersome and low yield chemical linking through disulfide bonding steps of Hudson render the combination of the references *prima facie* obvious for ordinary artisans motivated to streamline the production steps and costs of the production of recombinant proteins and the genetically engineered host cells that produce said proteins.

Applicant's arguments filed 2/8/06 have been fully considered but they are not persuasive. Applicant argues that protein C has a different sequence and cleavage site than the prorelaxin. This is unpersuasive because the amino acid sequence and cleavage sites do not have to be identical to the instant prorelaxin in order for the prior art enzyme to perform its function. If the prorelaxin has a cleavage site that the prior art enzyme can cleave, then the rejection is maintained for reasons of record. Whether the secretion pathway is regulated or constitutive does not seem to have a bearing on why the combined references do not render the instant invention obvious.

5. Claims 32-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hudson in view of Mulvihill and further in view of Thomas et al.(PTO-1449, filed 6/25/02, *PNAS* 88:5297-5301 (1991), "Thomas") for reasons of record and the following. The teachings of Hudson and Mulvihill are as set forth in **¶3** above. Hudson and Mulvihill do not teach host cells or methods using prohormone convertase 1 (PC1), also known as

PC3. Thomas does teach heterologous expression of transfected polypeptides with transfected PC1/PC3 and PC2. It would have been obvious at the time the invention was made for one of ordinary skill in the art to make isolated animal host cells that produced relaxin by using the sequence information from Hudson in the 293 cells as disclosed by Mulvihill with the PC1/PC3 and PC2 taught by Thomas because Thomas discloses that a combination of the different processing enzymes produces more efficient conversion of a prohormone into a mature hormone (abstract). Also, the many advantages taught by Mulvihill for the use of co-expression in mammalian cells as compared to single expression in mammalian cells (abstract, page 2, lines 4-41, and page 4, lines 32-37) would apply here too. Finally, the fact that the teachings of Mulvihill exclude the use of the cumbersome and low yield chemical linking through disulfide bonding steps of Hudson render the combination of the references *prima facie* obvious for ordinary artisans motivated to streamline the production steps and costs of the production of recombinant proteins and the genetically engineered host cells that produce said proteins.

Applicant's arguments filed 2/8/06 have been fully considered but they are not persuasive. Applicant argues that protein C has a different sequence and cleavage site than the prorelaxin. This is unpersuasive because the amino acid sequence and cleavage sites do not have to be identical to the instant prorelaxin in order for the prior art enzyme to perform its function. If the prorelaxin has a cleavage site that the prior art enzyme can cleave, then the rejection is maintained for reasons of record. Whether the

secretion pathway is regulated or constitutive does not seem to have a bearing on why the combined references do not render the instant invention obvious.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technical Center 1600 general number which is (571) 272-1600.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (571) 272-0883. The examiner can normally be reached on Monday to Friday from 0930 to 1800. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached at (571) 272-0867. The fax phone number for this Group is currently (571)-273-8300.

SG

Stephen Gucker

May 3, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER